trol) ± SEM for the 9 dogs.

	90 Min	3 Hours	8 Hours	24 Hours
Placebo	89 ± 7	82 ± 8	94 ± 10	79 ± 7
CGRP	*155 ± 22	*115 ± 9	*118 ± 12	*108 ± 15

* $p < 0.05$ vs. placebo

Despite a short half-life of less than 30 minutes, CGRP caused a significantly more rapid return of cardiac function from ischemia than placebo throughout the entire 24 hours of reperfusion. These results suggest that CGRP may improve recovery from reversible myocardial ischemia and may have unique properties as an intravenous inotrope in an intensive care unit setting because it does not appear to impair recovery from acute myocardial ischemia.

11:45

706-6 Endothelin-1 Receptor Antagonists BQ123 and BQ610 Delay Ischemic Contracture, Preserve High-Energy Phosphate Metabolism and Improve Systolic Function During Ischemia/Reperfusion

Hong Han, Barbara Braeker, Stefan Neubauer, Georg Ertl. *Department of Medicine, Würzburg University, FRG*

Using specific Endothelin-1 (ET-1) antagonists BQ123 and BQ610, we tested whether endogenous ET-1 contributes to ischemia/reperfusion injury in isolated, Langendorff-perfused rat hearts. BQ123 (7 μg/min) and BQ610 (1.75 μg/min) did not affect mechanical function or coronary flow and shifted the dose-response curve for ET-1 significantly to the right. Isovolumic rat hearts were pre-treated with BQ123, BQ610 or saline for 10 min, and were subjected to 30 min ischemia followed by reperfusion. At 15 min ischemia, the increase of left ventricular resting pressure (mmHg) was significantly reduced by BQ 123 (17 ± 3*; n = 11) and BQ610 (17 ± 3*; n = 12) compared to saline (45 ± 7; n = 12). During reperfusion, recovery of left ventricular developed pressure (mmHg) was improved with BQ123 (23 ± 7*) and BQ610 (20 ± 3*) compared to saline (10 ± 3). In hearts pre-treated with BQ610, high-energy phosphate metabolism was continuously recorded with 31P-NMR spectroscopy (7T Bruker NMR System). ATP content (% of control) at 30 min ischemia was higher with BQ610 (20 ± 3*; n = 11) compared to saline (5 ± 2; n = 8), and creatine phosphate recovery (% of control) was improved with BQ610 during reperfusion (76 ± 7* vs 54 ± 6 with saline). Thus, endogenous ET-1 contributes to ischemia/reperfusion injury. Specific ET-1 antagonists attenuate functional and metabolic consequences of ischemia/reperfusion injury without affecting pre-ischemic workload.

*$p < 0.05$ vs. saline.

707 Heart Failure: Clinical Trials

Monday, March 20, 1995, 10:30 a.m.–Noon
Ernest N. Morial Convention Center, La Louisiane A

10:30

707-1 Short-term ACE-Inhibition and Onset and Progression of Congestive Heart Failure in Patients with Acute Myocardial Infarction

Claudio Borghi, Ettore Ambrosioni, Bruno Magnani, SMILE Investigators. *University of Bologna, Bologna, Italy*

Anterior acute myocardial infarction (AMI) is often complicated by clinical signs of CHF. We report the data of 1146 patients with anterior A.M.I. without previous history or clinical signs of CHF on admission and enrolled under the *SMILE* study. Patients were randomly allocated to a 6-week double-blind treatment with placebo (P) or zofenopril (Z) and then followed-up for 1 year. Baseline demographic characteristics were similar in Z and P group who were comparable for blood pressure, ECG pattern, peak CPK, and concomitant drug treatment. After 6 weeks the cumulative occurrence of CHF was not different in Z and P groups (13.3% vs 13.9%; p = 0.234). Clinical signs of mild to moderate CHF were present in 11.7% of the Z population and 10.2% of the P group (P = 0.178) whereas severe refractory CHF occurred significantly less in Z (1.6%) compared to P (3.6%) patients (RR = 2.3: C.I. 95% 1–3.3: p = 0.0328). After 1 year the overall occurrence of CHF was 14.8% in P and 15.4% in Z treated patients. NYHA class I was more common among Z treated patients (8.2% vs 1.5%; p = 0.021) whereas the percentage of patients in NYHA class IV was higher in P treated patients (24.3% vs 11.0%; p = 0.001). In conclusion the early and long-term development and progression of CHF can be prevented by short-term administration of zofenopril in patients with acute myocardial infarction.

10:45

707-2 Effects of Carvedilol on Left Ventricular Function and Exercise Performance in Patients with Heart Failure of Ischemic Etiology

Stephen MacMahon, Robert Doughty, Norman Sharpe, ANZ Heart Failure Research Collaborative Group. *University of Auckland, Auckland, New Zealand*

Results from several small trials in patients with heart failure of predominantly idiopathic etiology suggest that beta-blocker therapy may improve ventricular function, but the effects on exercise performance remain less certain. To determine the effects of such treatment in patients with heart failure of ischemic etiology, patients with this condition and ejection fraction (EF) <45% were randomized to treatment with carvedilol (12.5–50 mg/day) or placebo. Prior to randomization, 444 patients entered a 2–3 week run-in phase on open label, low-dose carvedilol (6.25–12.5 mg/day). 415 patients (93%) were randomized. Primary outcome variables were radionuclide measurements of EF and measurements of treadmill exercise duration (TED) using a modified Naughton protocol. Secondary outcomes included left ventricular chamber dimensions measured by M-mode echocardiography, submaximal exercise performance assessed from 6 minute walk distance (6 MWD) and NYHA functional class. After 6 months, resting heart rate was reduced by 7.1 bpm, and blood pressure was reduced by 5.1/4.5 mmHg in the carvedilol group compared to the placebo group. Results for the main outcomes are shown below as differences between carvedilol and placebo groups after 6 months of follow-up.

LV Function and Size		Exercise and Symptoms	
EF	+5.0%*	TED	−23.6 s
LVEDD	−1.5 mm†	6 MWD	−7.7 m
LVESD	−2.6 mm*	NYHA	+0.1

*$p < 0.01$; †$p = 0.04$; all others NS. EF = ejection fraction, LV = left ventricular, EDD = end-diastolic dimension, ESD = end-systolic dimension

In conclusion, 6 months of treatment with carvedilol in patients with ischemic heart failure resulted in improved ejection fraction and reduced LV chamber dimensions. However, there were no detectable changes in maximal or submaximal exercise performance or in NYHA class.

11:00

707-3 CIBIS Left Ventricular Function Sub-study: Analysis of Predictive Factors of Initial Improvement and Prognostic Value

Philippe Lechat, Hervé Lardoux, Jean-Pierre Boissel, Serge Witchitz, Martin Hetzel, Luigi Ciampricotti, Eric Chanton, Christian Mésenge, Patrice Jaillon, CIBIS Investigators. *CIBIS Coordinating Center, Pitié-Salpétrière Hospital, Paris, France*

During the Cardiac Insufficiency Bisoprolol Study (CIBIS) which evaluated beta-blockade (BB) effects on mortality in 641 patients (pts) with heart failure (mean follow up: 1.9 ± 0.8 years, SD), we studied the determinants of BB induced improvement of left ventricular function (LVF), the mechanism of which remains unclear. Echocardiographic assessment of LVF was performed at baseline (BL) in all patients and in a subgroup of 164 patients (83 on B, 81 on P) still alive 5 months after inclusion. All patients received a background diuretic and vasodilator therapy and were blindly randomized either to placebo (P) or to bisoprolol (B). Among these 164 pts, a similar proportion in both groups presented with left bundle branch block (23 on P, 22 on B, NS) or chronic atrial fibrillation (15 on P, 10 on B, NS). According to all recorded parameters at baseline, this subgroup of pts was representative of the entire CIBIS population. Results (means ± SD):

		EDD (cm)	ESD (cm)	FS (%)
BL	P	6.8 ± 0.9	5.7 ± 0.9	16.8 ± 4.6
	B	6.9 ± 0.8	5.8 ± 0.8	15.5 ± 5.0
5 M	P	6.8 ± 1.0	5.7 ± 1.0	16.8 ± 5.8
	B	6.7 ± 0.9	5.4 ± 1*	20.1 ± 7.0**

EDD = end diastolic diameter; ESD = end systolic diameter; FS = fractional shortening; * p = 0.07; ** p = 0.001

LVFS significantly improved on B at 5 months compared to P (LVFS variation was: −0.04 ± 5.5% with P and +4.6 ± 6.5% with B, $p < 0.001$). Such improvement was similar in ischemic and non ischemic pts. It was uncorrelated to other BL parameters and to B induced bradycardia (−18 ± 12 beats/min at 5 M), but it was significantly correlated with survival after the initial 5 month period (Cox model, 12 patients died on P, 7 on B, p = 0.01).

We conclude that echocardiographic LVFS improvement on B is an independent marker of BB action in heart failure appears uncorrelated to baseline parameters but is associated with a better prognosis.

MONDAY AM